LUPIN LIMITED

SAFETY DATA SHEET

Section 1: Identification

Section 1, Identification

Material	**Valsartan and Hydrochlorothiazide Tablet USP** **80 mg/12.5 mg, 160 mg/12.5 mg, 160 mg/25 mg, 320 mg/12.5 mg, 320 mg/25 mg**
Manufacturer	**Lupin Limited** Goa - 403 722 INDIA
Distributor	Lupin Pharmaceuticals, Inc. 111 South Calvert Street, Harborplace Tower, 21st Floor, Baltimore, Maryland 21202 United States Tel. 001-410-576-2000 Fax. 001-410-576-2221

Section 2: Hazard(s) Identification

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Fire and Explosion	Expected to be non-combustible.
Health	Valsartan and hydrochlorothiazide are contraindicated in patients who are hypersensitive to any component of this product. Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs. Do not coadminister aliskiren with valsartan and hydrochlorothiazide tablets in patients with diabetes.
Environment	No information is available about the potential of this product to produce adverse environmental effects.

Section 3: Composition/Information on Ingredients

Section 3, Composition/information on ingredients

Ingredients	**CAS**
Valsartan USP	137862-53-4
Hydrochlorothiazide USP	00058-93-5

Section 4: First-Aid Measures

Section 4, First-aid measures

Ingestion	Get medical attention. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Inhalation	Remove to fresh air, If not breathing, give artificial respiration. Get medical attention.
Skin Contact	Wash off immediately with plenty of water. Continue to rinse for at least 15 minutes. Immediately take off all contaminated clothing. Get medical attention if irritation develops and persists.
Eye Contact	Immediately flush eyes with water for at least 15 minutes. If irritation occurs or persist, get medical attention.

NOTES TO HEALTH PROFESSIONALS

Medical Treatment	Treat according to locally accepted protocols. For additional guidance, refer to the current prescribing information or to the local poison control information center. Protect the patient's airway and support ventilation and perfusion. Meticulously monitor and maintain, within acceptable limits, the patient's vital signs, blood gases, serum electrolytes, etc.
OVERDOSAGE	Limited data are available related to overdosage in humans. The most likely manifestations of overdosage would be hypotension and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. Depressed level of consciousness, circulatory collapse and shock have been reported. If symptomatic hypotension should occur institute supportive treatment. Valsartan is not removed from the plasma by dialysis. The degree to which hydrochlorothiazide is removed by hemodialysis has not been established. The most common signs and symptoms observed in patients are those caused by electrolyte depletion (hypokalemia, hypochloremia, hyponatremia) and dehydration resulting from excessive diuresis. If digitalis has also been administered, hypokalemia may accentuate cardiac arrhythmias. In rats and marmosets, single oral doses of valsartan up to 1524 and 762 mg/kg in combination with hydrochlorothiazide at doses up to 476 and 238 mg/kg, respectively, did not show any adverse treatment-related effects. These no adverse effect doses in rats and marmosets, respectively, represent 46.5 and 23 times the MRHD of valsartan and 188 and 113 times the MRHD of hydrochlorothiazide on a mg/m^2 basis. (Calculations assume an oral dose of 320 mg/day valsartan in combination with 25 mg/day hydrochlorothiazide and a 60-kg patient.) Valsartan was without grossly observable adverse effects at single oral doses up to 2000 mg/kg in rats and up to 1000 mg/kg in marmosets, except for salivation and diarrhea in the rat and vomiting in the marmoset at the highest dose (60 and 31 times, respectively, the MRHD on a mg/m^2 basis) (Calculations assume an oral dose of 320 mg/day and a 60-kg patient). The oral LD_{50} of hydrochlorothiazide is greater than 10 g/kg in both mice and rats, which represents 2027 and 4054 times, respectively, the MRHD on a mg/m^2 basis. (Calculations assume an oral dose of 25 mg/day and a 60-kg patient.).

Section 5: Fire-Fighting Measures

Section 5, Fire-fighting measures

Fire and Explosion Hazards	Assume that this product is capable of sustaining combustion.
Extinguishing Media	Water spray, carbon dioxide, dry chemical powder or appropriate foam.

Special Firefighting Procedures	For single units (packages): No special requirements needed. For larger amounts (multiple packages/pallets) of product: Since toxic, corrosive or flammable vapors might be evolved from fires involving this product and associated packaging, self-contained breathing apparatus and full protective equipment are recommended for firefighters.
Hazardous Combustion Products	Hazardous combustion or decomposition products are expected when the product is exposed to fire.

Section 6: Accidental Release Measures

Section 6, Accidental release measures

Personal Precautions	Wear suitable protective clothing, gloves and eye/face protection.
Environmental Precautions	Avoid release to the environment.
Clean-up Methods	Collect and place it in a suitable, properly labeled container for recovery or disposal.

Section 7: Handling and Storage

Section 7, Handling and storage

Handling	Minimize dust generation and accumulation. If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment. Wash hands and any exposed skin.
Storage	Store at 20°C - 25°C (68°F-77°F); excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature]. Protect from moisture. Dispense in tight container (USP).

Section 8: Exposure Controls/Personal Protection

Section 8, Exposure controls/personal protection

Wear appropriate clothing to avoid skin contact. Wash hands and arms thoroughly after handling.

Section 9: Physical and Chemical Properties

Section 9, Physical and chemical properties

Valsartan and hydrochlorothiazide tablets USP are available as non-scored tablets containing valsartan/hydrochlorothiazide 80 mg/12.5 mg, 160 mg/12.5 mg, 160 mg/25 mg, 320 mg/12.5 mg and 320 mg/25 mg. Strengths are available as follows.

80 mg/12.5 mg Tablet - Light pink colored, capsule shaped, film-coated biconvex tablets, debossed with “LU” on one side and “P11” on the other side.

Bottles of 90	NDC 68180-103-09
Bottles of 500	NDC 68180-103-02
Bottles of 1000	NDC 68180-103-03
10 X 10’ Blister Pack	NDC 68180-103-13

160 mg/12.5 mg Tablet - Reddish brown colored, capsule shaped, film-coated biconvex tablets, debossed with “LU” on one side and “P12” on the other side.

Bottles of 90	NDC 68180-104-09
Bottles of 500	NDC 68180-104-02
Bottles of 1000	NDC 68180-104-03
10 X 10’ Blister Pack	NDC 68180-104-13

160 mg/25 mg Tablet - Light orange colored, capsule shaped, film-coated biconvex tablets, debossed with “LU” on one side and “P13” on the other side.

Bottles of 90	NDC 68180-105-09
Bottles of 500	NDC 68180-105-02
Bottles of 1000	NDC 68180-105-03
10 X 10’ Blister Pack	NDC 68180-105-13

320 mg/12.5 mg Tablet - Pink, capsule shaped, film-coated biconvex tablets, debossed with “LU” on one side and “P14” on the other side.

Bottles of 90	NDC 68180-101-09
Bottles of 500	NDC 68180-101-02
10 X 10’ Blister Pack	NDC 68180-101-13

320 mg/25 mg Tablet - Yellow, capsule shaped, film-coated biconvex tablets, debossed with ‘LU’ on one side and ‘P15’ on the other side.

Bottles of 90	NDC 68180-102-09
Bottles of 500	NDC 68180-102-02
10 X 10’ Blister Pack	NDC 68180-102-13

Section 10: Stability and Reactivity

Section 10, Stability and reactivity

The product is stable and non-reactive under normal conditions of use, storage and transport.

Section 11: Toxicological Information

Section 11, Toxicological information

Carcinogenesis, Mutagenesis, Impairment of Fertility

Valsartan-Hydrochlorothiazide
No carcinogenicity, mutagenicity, or fertility studies have been conducted with the combination of valsartan and hydrochlorothiazide. However, these studies have been conducted for valsartan as well as hydrochlorothiazide alone. Based on the preclinical safety and human pharmacokinetic studies, there is no indication of any adverse interaction between valsartan and hydrochlorothiazide.

Valsartan
There was no evidence of carcinogenicity when valsartan was administered in the diet to mice and rats for up to 2 years at doses up to 160 and 200 mg/kg/day, respectively. These doses in mice and rats are about 2.6 and 6 times, respectively, the MRHD on a mg/m^2 basis (Calculations assume an oral dose of 320 mg/day and a 60-kg patient).

Mutagenicity assays did not reveal any valsartan-related effects at either the gene or chromosome level. These assays included bacterial mutagenicity tests with *Salmonella* (Ames) and *E. coli*; a gene mutation test with Chinese hamster V79 cells; a cytogenetic test with Chinese hamster ovary cells; and a rat micronucleus test.

Valsartan had no adverse effects on the reproductive performance of male or female rats at oral doses up to 200 mg/kg/day. This dose is about 6 times the MRHD on a mg/m^2 basis (Calculations assume an oral dose of 320 mg/day and a 60-kg patient).

Hydrochlorothiazide
Two-year feeding studies in mice and rats conducted under the auspices of the National Toxicology Program (NTP) uncovered no evidence of a carcinogenic potential of hydrochlorothiazide in female mice (at doses of up to approximately 600 mg/kg/day) or in male and female rats (at doses of up to approximately 100 mg/kg/day). The NTP, however, found equivocal evidence for hepatocarcinogenicity in male mice.

Hydrochlorothiazide was not genotoxic *in vitro* in the Ames mutagenicity assay of *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538 and in the Chinese Hamster Ovary (CHO) test for chromosomal aberrations, or *in vivo* in assays using mouse germinal cell chromosomes, Chinese hamster bone marrow chromosomes, and the Drosophila sex-linked recessive lethal trait gene. Positive test results were obtained only in the *in vitro* CHO Sister Chromatid Exchange (clastogenicity) and in the Mouse Lymphoma Cell (mutagenicity) assays, using concentrations of hydrochlorothiazide from 43 to 1300 mcg/mL, and in the Aspergillus Nidulans non-disjunction assay at an unspecified concentration.

Hydrochlorothiazide had no adverse effects on the fertility of mice and rats of either sex in studies wherein these species were exposed, via their diet, to doses of up to 100 and 4 mg/kg, respectively, prior to mating and throughout gestation. These doses of hydrochlorothiazide in mice and rats represent 19 and 1.5 times, respectively, the MRHD on a mg/m^2 basis. (Calculations assume an oral dose of 25 mg/day and a 60-kg patient.)

Section 12: Ecological Information

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No relevant studies identified.

Section 13: Disposal Considerations

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Incinerate in an approved facility. Follow all federal state and local environmental regulations.

Section 14: Transport Information

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IATA/ICAO - Not Regulated

IATA Proper shipping Name	:	N/A
IATA UN/ID No	:	N/A

IATA Hazard Class	:	N/A
IATA Packaging Group	:	N/A
IATA Label	:	N/A

IMDG - Not Regulated

IMDG Proper shipping Name	:	N/A
IMDG UN/ID No	:	N/A
IMDG Hazard Class	:	N/A
IMDG Flash Point	:	N/A
IMDG Label	:	N/A

DOT - Not Regulated

DOT Proper shipping Name	:	N/A
DOT UN/ID No	:	N/A
DOT Hazard Class	:	N/A
DOT Flash Point	:	N/A
DOT Packing Group	:	N/A
DOT Label	:	N/A

Section 15: Regulatory Information

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This Section Contains Information relevant to compliance with other Federal and/or state laws.

Section 16: Other Information

Section 16, Other information

The above information is believed to be correct but does not purport to be all-inclusive and shall be used only as a guide. Nothing herein shall be deemed to create any warranty, express or implied. It is the responsibility of the user to determine the applicability of this information and the suitability of the material or product for any particular purpose.

Lupin shall not be held liable for any damage resulting from handling or from contact with the above product. Lupin reserves the right to revise this SDS.